REMARKS

Status of Claims and Support for Amendments

Claims 1-4 and 7 are cancelled without prejudice or disclaimer. Claims 5-6 and 8-10 are amended. New claims 12-13 are added.

No new matter is introduced by virtue of the within amendments; support therefor can be found throughout the specification and original claims. For instance, support for the subject matter, "a vascular disorder resulting from uric acid uptake or elimination into vascular smooth muscle cells" may be found, *inter alia*, in the description at paragraphs [0008] and [0026]. Support for amended claim language which recites "measuring the level of uric acid uptake or elimination in the [vascular smooth muscle] cell" is found, *inter alia*, at Example 1 ([0038] and [0039]) in the description. "Measuring the proliferation ability of the [vascular smooth muscle] cell" is based, *inter alia*, on the description in Example 2 ([0040]). "Measuring the amount of a monocyte chemotactic factor produced by the cell" is based, *inter alia*, on the description in Example 3 ([0041]). Support for new claims 12-13 can be found in Example 8 ([0051]) and Fig.15, i.e., "umbilical vein epithelial cells" can be used as a "vascular smooth muscle cell." Support for new claim 14 can be found in paragraph [0027].

Priority

The first paragraph of the specification has been amended to recite relevant domestic priority data.

Additionally, the Office Action acknowledges Applicants' claim to priority under 35 USC 119(a) - (d). Accordingly, in order to obtain the benefit(s) of foreign priority, submitted herewith is a verified English translation of JP 2003-384863, as filed with the Japanese Patent Office on November 14, 2003. With the filing of the verified translation, Applicants can rely on the priority date of November 14, 2003, to overcome the art rejections (discussed below).

Claims Rejections under 35 USC §112, 2nd paragraph

Claims 5-11 are rejected under 35 USC §112, 2nd paragraph, as allegedly being indefinite. The Office Action asserts that "it is unclear if the cell line is expressing URAT1 in the presence of a test compound, in the absence of it or is expressing it constitutively." Office Action, page 3. Additionally, objection is made to Applicants' method claims in that they lack positive steps as well as a step concluding the result of the method. Further, the dependency recited in claim 6 is indicated as being improper.

Applicants have amended the claims to clarify the features of the invention and address the noted informalities. As amended, each of the pending claims involves contacting a vascular smooth muscle cell with urate. Also, each of the claims as currently presented includes positive steps and a concluding step. Lastly, claim 6 is amended to recite a proper dependency.

Reconsideration and withdrawal of the rejection under 35 USC §112, 2nd paragraph, are requested.

Rejection under 35 USC §102(b)

Claims 5-7 are rejected under 35 USC §102(b) over Endou et al. (CA 2456172, published April 3, 2003) ("Endou").

The rejection is respectfully traversed.

Applicants herewith submit a verified translation of the Japanese priority document which was filed on November 14, 2003 (less than 1 year from the publication date of Endou et al.). The priority application fully supports the present claims. Accordingly, Endou may not properly be applied against the present application under 35 USC §102(b).

Furthermore, Applicants respectfully submit that Endou does not anticipate the present invention because the reference does not teach each and every element of claims 5-7.

As an initial matter, claim 7 has been cancelled, thereby rendering the rejection moot with respect to this claim. Claims 5 and 6 as currently presented are directed to a method for screening a substance efficacious for healing, preventing or treating vascular disorders resulting from abnormal uric acid uptake or elimination by URAT1 into a vascular smooth muscle cell comprising, *inter alia*, contacting a vascular smooth muscle cell with a test compound and urate. In contrast, the Examiner alleges that "Endou et al. teach a novel urate transporter gene participating in the urate transport in the kidney and a urate transporter which is a polypeptide encoded by the above gene." Office Action, page 4. The cited reference, however, does not disclose a method for screening a substance using a vascular smooth muscle, as required in the present invention.

Accordingly, for at least the above reasons, reconsideration and withdrawal of the rejection are requested.

Rejection under 35 USC §103(a)

Claims 8-12 are rejected under 35 USC §103(a) over Endou in view of Kanellis et al. (*Hypertension*: 41, 1287-1293, 2003) ("Kanellis") and Hurteau et al. (*Cancer*, 74, 93-99, 1994) ("Hurteau").

The rejection is respectfully traversed.

As noted above, Applicants herewith submit a verified translation of the Japanese priority document which was filed on November 14, 2003 (less than 1 year from the publication date of Endou). The priority application fully supports the present claims. Accordingly, Endou may not properly be applied as a 102(b) reference against the present application under 35 USC 103(a).

Kanellis and Hurteau cannot sustain the rejection. Indeed, the Examiner relies on these two references in a secondary capacity to allegedly remedy certain deficiencies of Endou (Office Action, pages 6-7).

Furthermore, after reviewing Endou, Kanellis and Hurteau, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness because a person of ordinary skill in the art would not have arrived at the claimed invention based on the teachings of the cited references. Claims 8-12 as currently presented are directed to methods for screening a substance efficacious for healing, preventing or treating vascular disorders resulting from abnormal uric acid uptake or elimination by URAT1 comprising, *inter alia*, contacting a vascular smooth muscle cell with a test compound and urate. As discussed above, Endou does not disclose a method for screening a substance using a vascular smooth muscle cell, as required in the present invention.

Kanellis and Hurteau do not cure the deficiencies of Endou. The Examiner has characterized Kanellis as allegedly disclosing "that soluble uric acid can induce vascular smooth muscle proliferation, activated through ERK, MAPK[,] Cox-2 or PDGF pathways." Office Action, page 7. Hurteau allegedly "exemplif[ies] a well known and routine[] use of thymidine incorporation assay for determining cell proliferation." *Id.* Neither reference, however, teaches a method for screening a substance using a vascular smooth muscle cell, as required in the present invention.

Moreover, the United States Patent and Trademark Office has published Examination Guidelines to aid Examiners in formulating obviousness rejections. *See Examination Guidelines for Determining Obviousness under 35 U.S.C. 103 in view of the Supreme Court decision in KSR International v. Teleflex Inc.*, Fed. Reg. Vol. 72, pp. 57526 to 57535 (October 10, 2007) (hereinafter "the Examination Guidelines"). Seven rationales are suggested by which obviousness may be found, *e.g.*, by combining elements in the art or substituting one known element for another. As a common thread through all the rationales, the Examiner must establish on the record that a person of ordinary skill in the art would have recognized that the results of the combination or substitution were predictable. *See id.* at 57529.

The Examiner has not met the burden because as of the filing date of the present application, there was no reasonable expectation that URAT1 is expressed in

vascular smooth muscle cells. At the time of filing, it was known that organs, such as kidneys, have various organic anion transporters that participate in uptake and excretion of uric acid, including OAT1, OAT3, and URAT1. However, a vessel comprising vascular smooth muscle cells is not an organ. It would not have been predictable that such a vessel would express URAT1.

In addition, there was no reasonable expectation that one of ordinary skill in the art could treat vascular disorders not induced by hyperuricemia. Applicants were the first to show that vascular smooth muscle cells only express URAT1. See Specification, paragraphs [0042]-[0047] and Figure 11. The absence of additional OAT transporters is significant because abnormally-increased uric acid uptake or abnormally-decreased uric acid elimination by URAT1 immediately results in an increase in the amount of uric acid present in regions peripheral to the URAT1. The presence of the excess uric acid also causes increased production of MCP-1, which further stimulates the vascular wall. Under these conditions, vascular wall disorders can develop even when uric acid is within normal levels in the blood (i.e., vascular wall disorders not induced by hyperuricemia). In contrast, this phenomenon does not occur in organs, such as kidneys, because additional uric acid transporters are present that function to uptake and eliminate uric acid within normal uric acid levels.

Applicants were the first to discover that i) URAT1 is expressed in vascular smooth muscle cells; ii) URAT1 participates in transportation of uric acid from blood to smooth muscle cells; and iii) URAT1 plays an important role in the development of vascular disorders, including hyperuricemia-independent vascular disorders. See Specification, paragraph [0008] and Examples 1-9. Prior to Applicants discovery, one of ordinary skill in the art would not have been motivated to use a vascular smooth muscle cell in the claimed methods. Furthermore, without an express teaching that abnormality of URAT1 in vascular smooth muscle cells is a true and direct cause of vascular disorders, one of ordinary skill in the art would not have reasonably expected to successfully practice the claimed invention.

For at least the above reasons, the Examiner has not established a *prima facie* case of obviousness. Accordingly, reconsideration and withdrawal of the rejection are requested.

Double Patenting

Claims 5-7 are rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of USP 7,510,847 ("the '847 patent"). The Office Action acknowledges that the conflicting claims are not identical. However, the position is taken that the claims are not patentably distinct from one another "because the transporter used in the method of screening of the patent is the same and the method has the same outcome as in the instant Application". Office Action, pages 8-9. Applicants respectfully disagree and traverse this rejection. Applicants respectfully assert that the claims of the '847 patent neither anticipate nor render obvious the presently claimed invention.

As noted in MPEP § 804(III), "a double patenting rejection must rely on a comparison with the *claims* in an issued or to be issued patent, whereas an anticipation or obviousness rejection based on the same patent under 35 U.S.C. 102(e)/ 103(a) relies on a comparison with what is disclosed (whether or not claimed) in the same issued or to be issued patent." (emphasis added; formatting removed). Furthermore, inventions based on the identification or selection of a specific material or compound with particularly desirable properties within a previously claimed genus of such materials or compounds are patentably distinct from the prior claimed subject matter. *See e.g.*, *In re Kaplan*, 789 F.2d 1574, 1578, 1580 (Fed. Cir. 1986) (prior generic patent claim did not invalidate claim to later selected species for double patenting); *see also In re Ruschig*, 343 F.2d 965, 974-75 (C.C.P.A. 1965) (prior generic disclosure did not anticipate later selected species under 35 U.S.C. § 102); *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1340 (Fed. Cir. 2003) ("Improvement and selection inventions are ubiquitous in patent law . . ."); *In re Baird*, 16 F.3d 380, 383 (Fed. Cir. 1994) (prior generic disclosure did not render later selected species obvious under 35 U.S.C. § 103).

As described above, claims 5-7 are directed to, *inter alia*, methods for screening a substance efficacious for healing, preventing or treating vascular disorders resulting from abnormal uric acid uptake or elimination by URAT1 comprising, *inter alia*, contacting a vascular smooth muscle cell with a test compound and urate. In contrast, claims 1-6 of the '847 patent are not directed to this subject matter. Nothing in the '847 patent claims even suggests a screening method using a vascular smooth muscle cell. In the absence of an express or inherent disclosure of a screening method using a vascular smooth muscle cell, the instant claims simply cannot be anticipated. Likewise, there is no disclosure in the prior claims that provides a reason to associate URAT1 with vascular smooth muscle cells. Accordingly, as claims 1-6 of the '847 patent do not teach every element set forth in claims 5-7 of the present application, claims 1-6 of the '847 patent do not anticipate or render obvious claims 5-7 of the present application.

For at least the above reasons, it is respectfully submitted that the present invention is patentably distinct from the '847 patent.

Reconsideration and withdrawal of the rejection are requested.

CONCLUSION

In view of the above amendments and remarks, Applicants believe the pending application is in condition for allowance.

PETITION FOR EXTENSION AND FEE AUTHORIZATION

Applicant requests a 1 month extension of time to file the within response. The Commissioner is authorized to charge the extension fee, extra claim fees and any other fees required in connection with this submission to our Deposit Account, No. 04-1105, Reference 65445(71526). Any overpayments should be credited to said Deposit Account.

Dated: June 7, 2011

Respectfully submitted,
Electronic signature: / Kellie K. DiNapoli, Ph.D., Esq./
Kellie K. DiNapoli, Ph.D., Esq.
Registration No.: 61,455

Customer No. 21874

Christine C. O'Day
Registration No.: 38,256
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 517-5555
Attorneys/Agents for Applicants